

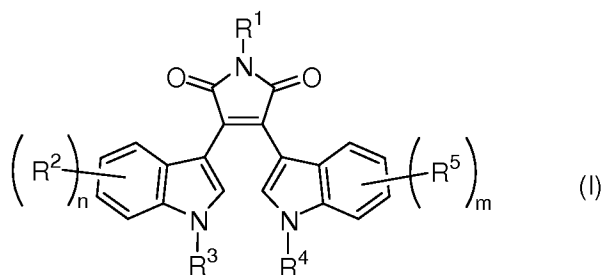
b.) Amendment to the Claims:

Claims 1-3 (Cancelled).

4. (Currently Amended) ~~The method according to any one of claims 1 to 3~~ A method of manufacturing a Tuj1 positive neuron which comprises culturing a neural stem cell in the presence of a substance that inhibits glycogen synthase kinase-3 (GSK-3) to allow neogenesis of the neuron, and collecting the neuron from the culture, wherein the substance that inhibits the activity of GSK-3 is lithium or a pharmacologically acceptable salt thereof.

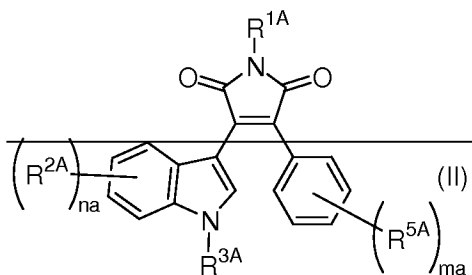
5. (Currently Amended) ~~The method according to any one of claims 1 to 3~~ A method of manufacturing a Tuj1 positive neuron which comprises culturing a neural stem cell in the presence of a substance that inhibits glycogen synthase kinase-3 (GSK-3) to allow neogenesis of the neuron, and collecting the neuron from the culture, wherein the substance that inhibits the activity of GSK-3 comprises a bisindolylmaleimide derivative, a 3-aryl-4-indolylmaleimide derivative, an indolocarbazole derivative, an indolo[3,2-d][1]benzazepin-6(5H)-one derivative or an indirubin derivative, or a pharmacologically acceptable salt thereof.

6. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 5, wherein the ~~substance that inhibits the activity of GSK-3~~ compound bisindolylmaleimide derivative is represented by the formula (I):



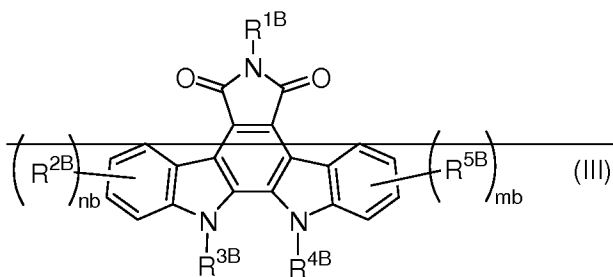
[wherein n and m ~~may be the same or different, and~~ independently represent an integer of 1 to 3; R¹, R³ and R⁴ ~~may be the same or different, and~~ independently represent hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, -COR⁶ (wherein R⁶ represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl), -COOR⁷ (wherein R⁷ represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl) or -OR⁸ (wherein R⁸ represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl); R² and R⁵ ~~may be the same or different, and~~ independently represent hydrogen, substituted or unsubstituted lower alkyl, a substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxy carbonyl, substituted or unsubstituted aryl, carboxy, halogen, hydroxy, nitro, amino, or mono- or di-lower alkylamino; and when n and m are 2 or 3, each of R² and R⁵ may be the same or different],

~~a compound represented by the formula (II):~~

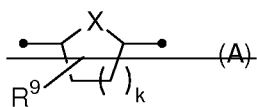


(wherein na, ma, R^{1A} , R^{2A} , R^{3A} and R^{5A} are as defined for the
aforementioned n, m, R^1 , R^2 , R^3 and R^5 , respectively, or

a compound represented by the formula (III):



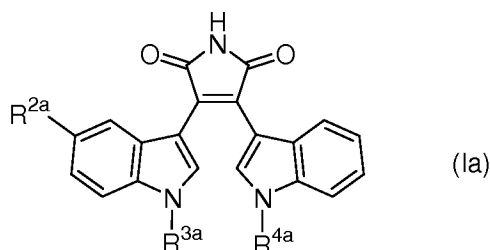
[wherein nb, mb, R^{1B} , R^{2B} and R^{5B} are as defined for the aforementioned n,
m, R^1 , R^2 and R^5 , respectively; R^{3B} and R^{4B} may be the same or different, and represent
hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower
alkenyl, $-COR^6$, $-COOR^7$ or $-OR^8$, or R^{3B} and R^{4B} together form



(wherein k represents 1 or 2; X represents CH_2 , NH, an oxygen atom or a
sulfur atom; R^9 represents hydroxy, carboxy, carbamoyl or lower alkoxy carbonyl)];

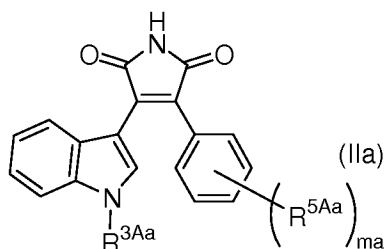
or a pharmacologically acceptable salt thereof.

7. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 6, wherein the ~~substance that inhibits the activity of GSK-3 is a compound~~ bisindolylmaleimide derivative is represented by the formula (Ia):



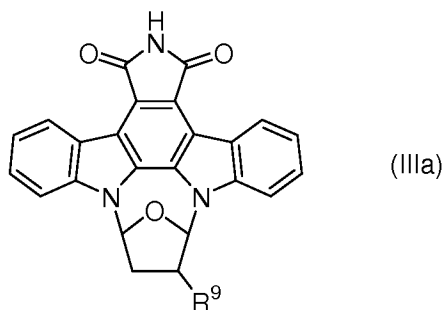
(wherein R^{2a} represents hydrogen, lower alkoxy, lower alkoxycarbonyl, aryl or nitro; and R^{3a} and R^{4a} ~~may be the same or different, and~~ independently represent substituted or unsubstituted lower alkyl),
or a pharmacologically acceptable salt thereof.

8. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 44, wherein the ~~substance that inhibits the activity of GSK-3 is a compound~~ bisindolylmaleimide derivative is represented by the formula (IIa):



(wherein R^{3Aa} represents substituted or unsubstituted lower alkyl; and R^{5Aa} represents halogen),
or a pharmacologically acceptable salt thereof.

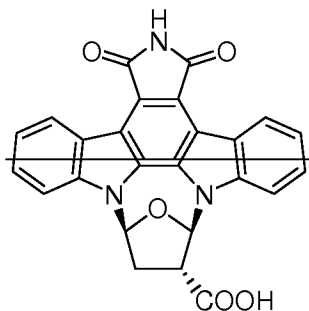
9. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 47, wherein the ~~substance that inhibits the activity of GSK-3 is a compound~~ indolocarbazole derivative is represented by the formula (IIIa):



or ~~or~~ a pharmacologically acceptable salt thereof.

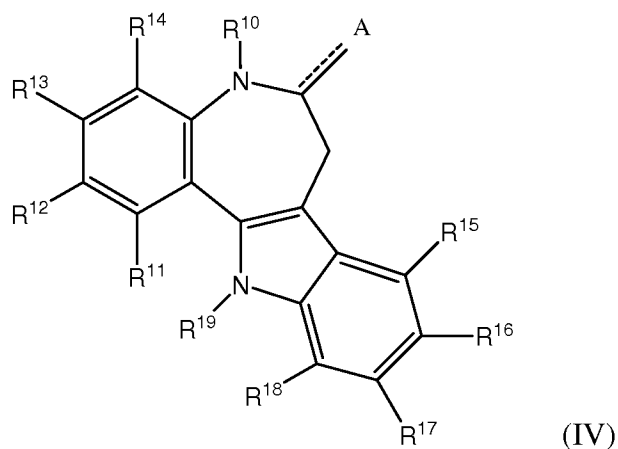
10. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 6, wherein the ~~substance that inhibits the activity of GSK-3 is a compound~~ bisindolylmaleimide derivative is selected from the group consisting of 3,4-bis(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-(1-methylindole-3-yl)-4-(1-propylindole-3-yl)-1H-pyrrole-2,5-dione, 3-[1-(3-cyanopropyl)indole-3-yl]-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-[1-(3-aminopropyl)indole-3-yl]-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-[1-(3-carboxypropyl)indole-3-yl]-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-[1-(3-carbamoylpropyl)indole-3-yl]-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-[1-(3-aminopropyl)indole-3-yl]-4-(1-methyl-5-propyloxyindole-3-yl)-1H-pyrrole-2,5-dione, 3-[1-(3-hydroxypropyl)indole-3-yl]-4-(1-methyl-5-phenylindole-3-yl)-1H-pyrrole-2,5-dione, 3-[1-(3-aminopropyl)indole-3-yl]-4-(1-methyl-5-phenylindole-3-yl)-1H-pyrrole-2,5-dione, 3-[1-(3-hydroxypropyl)indole-3-yl]-4-(1-methyl-5-methoxycarbonylindole-3-yl)-1H-pyrrole-2,5-dione, 3-[1-(3-hydroxypropyl)indole-3-yl]-4-

(1-methyl-5-nitroindole-3-yl)-1H-pyrrole-2,5-dione, and 3-(1-methylindole-3-yl)-4-[1-(3-hydroxypropyl)-5-nitroindole-3-yl]-1H-pyrrole-2,5-dione, ~~3-(2-chlorophenyl)-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-(2,4-dichlorophenyl)-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-(2-chlorophenyl)-4-[1-(3-hydroxypropyl)indole-3-yl]-1H-pyrrole-2,5-dione, 4-[1-(3-aminopropyl)indole-3-yl]-3-(2-chlorophenyl)-1H-pyrrole-2,5-dione and~~



or ~~or~~ a pharmacologically acceptable salt thereof.

11. (Currently Amended) ~~The method according to any one of claims 1 to 3~~ A method of manufacturing a Tuj1 positive neuron which comprises culturing a neural stem cell in the presence of a substance that inhibits glycogen synthase kinase-3 (GSK-3) to allow neogenesis of the neuron, and collecting the neuron from the culture, wherein the substance that inhibits the activity of GSK-3 comprises is a compound represented by the formula (IV):



[wherein A is oxygen or sulfur coupled to the right by a single or double bond; R¹⁰ is selected from the group consisting of hydrogen, aryl, lower aliphatic substituents, particularly alkyl and lower alkyl ester; R¹¹-R¹⁴ are independently selected from the group consisting of alkoxy, amino, acyl, aliphatic substituents, particularly alkyl, alkenyl and alkynyl substituents, aliphatic alcohols, particularly alkyl alcohols, aliphatic nitriles, particularly alkyl nitriles, cyano, nitro, carboxyl, halogen, hydrogen, hydroxyl, imino and α,β -unsaturated ketones; R¹⁵-R¹⁸ are independently selected from the group consisting of aliphatic substituents, particularly alkyl, alkenyl and alkynyl substituents, particularly lower aliphatic substituents, aliphatic alcohols, particularly alkyl alcohols, alkoxy, acyl, cyano, nitro, epoxy, haloalkyl groups, halogen, hydrogen and hydroxyl; and R¹⁹ is selected from the group consisting of aliphatic groups, particularly lower alkyl groups, aliphatic alcohols, particularly alkyl alcohols, carboxylic acids and hydrogen], or a pharmacologically acceptable salt thereof.

12. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 11, wherein the substance that inhibits the activity of GSK-3 is a compound selected from the group consisting of 7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one,

2-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 10-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-bromo-6,11-dihydro-thieno[3',2':2,3]azepino[4,5-b]indol-5(4H)-one, 9-bromo-7,12-dihydro-4-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-4-hydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-4-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dihydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dimethoxy-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-bromo-7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-indolo[3,2d][1]benzazepin-6(5H)-thione, 9-bromo-5,12-bis-(t-butyloxycarbonyl)-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-12-(t-butyloxycarbonyl)-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-5,7-bis-(t-butyloxycarbonyl)-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-5,7,12-tri-(t-butyloxycarbonyl)-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-5-methyloxycarbonylmethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-12-methyloxycarbonylmethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-12-(2-hydroxyethyl)-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,9-dibromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8,10-dichloro-7,12-dihydro-indolo[3,2d][1]benzazepin-6(5H)-one, 9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-

6(5H)-one, 9-bromo-7,12-dihydro-5-methyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 5-benzyl-9-bromo-7,12-dihydro-5-methyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-12-methyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-12-ethyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-12-(2-propenyl)-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-9-methyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-9-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-fluoro-7,12-dihydro-12-(2-propenyl)-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-bromo-7,12-dihydro-indolo[3,2d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2-(methyliminoamine)-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2-(carboxylic acid)-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-10-hydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-11-hydroxymethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-4-hydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dihydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,3-dimethoxy-9-nitro-7,12-dihydro-indolo[3,2d][1]benzazepin-6(5H)-one, 9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,3-dimethoxy-9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-nitro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 3-(6-oxo-9-trifluoromethyl-5,6,7,12-tetrahydro-indolo[3,2-d][1]benzazepin-2-yl)-propionitrile, 2-bromo-9-nitro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 3-(6-oxo-9-trifluoromethyl-5,6,7,12-tetrahydro-indolo[3,2-d][1]benzazepin-2-yl)acrylonitrile, 2-(3-hydroxy-1-propenyl)-9-trifluoromethyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-iodo-9-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-(3-oxo-1-butenyl)-9-trifluoromethyl-7,12-tetrahydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-chloro-6,11-

dihydro-thieno[3',2':2,3]azepino[4,5-b]indol-5(4H)-one, 2-iodo-9-trifluoromethyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-pyrido[3',2':4,5]pyrrolo[3,2-d][1]benzazepin-6(5H)-one, 11-methyl-7,12-dihydro-indolo[3,2-d][1]-benzazepin-6(5H)-one, 2-[2-(1-hydroxycyclohexyl)ethinyl]-9-trifluoromethyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-iodo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-ethyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-methyl-6,11-dihydro-thieno[3',2':2,3]azepino[4,5-b]indol-5(4H)-one and 3-(6-oxo-9-trifluoromethyl-5,6,7,12-tetrahydro-indolo[3,2-d][1]benzazepin-2-yl)acrylic acid, methyl acid methyl ester, or a pharmacologically acceptable salt thereof.

13. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 11, wherein the substance that inhibits the activity of GSK-3 is selected from the group consisting of 9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-bromo-7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dimethoxy-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,9-dibromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-bromo-6,11-dihydro-thieno[3',2':2,3]azepino[4,5-b]indole-5(4H)-one, 7,12-dihydro-9-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 10-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-

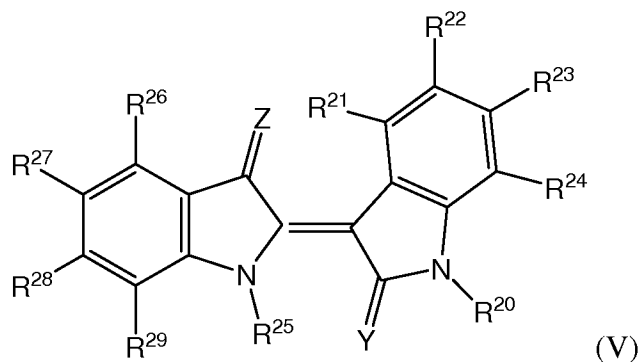
one, 9-fluoro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-methyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-thione, 8,10-dichloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-12-(2-hydroxyethyl)-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dihydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-12-methyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-5-methyloxycarbonylmethyl-indolo[3,2-d][1]benzazepin-6(5H)-one and 7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, or a pharmacologically acceptable salt thereof.

14. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 11, wherein the substance that inhibits the activity of GSK-3 is selected from the group consisting of 9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-bromo-7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dimethoxy-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,9-dibromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-bromo-6,11-dihydro-thieno[3',2':2,3]azepino[4,5-b]indol-5(4H)-one, 7,12-dihydro-9-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, or a pharmacologically acceptable salt thereof.

15. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 11, wherein the substance that inhibits the activity of GSK-3 is 9-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, or

a pharmacologically acceptable salt thereof.

16. (Currently Amended) ~~The method according to any one of claims 1 to 3~~ A method of manufacturing a Tuj1 positive neuron which comprises culturing a neural stem cell in the presence of a substance that inhibits glycogen synthase kinase-3 (GSK-3) to allow neogenesis of the neuron, and collecting the neuron from the culture, wherein the substance that inhibits the activity of GSK-3 ~~comprises~~ is a compound represented by the formula (V):



[wherein R²⁰ and R²⁵ ~~may be the same or different and~~ independently represent hydrogen; halogen; a hydroxy group; a methylene hydroxy group; a straight or branched C₁ to C₁₈-alkyl or straight or branched C₁ to C₁₈-alkoxy or a methylenealkoxy group (wherein the alkoxy is straight or branched C₁ to C₁₈); a cycloalkyl group having 3 to 7 carbon which may have one or more ~~heteroatoms~~ heteroatoms; a substituted or unsubstituted aryl, aralkyl or aryloxy group which may have one or more heteroatoms; a mono-, di- or trialkylsilyl group each independently having 1 to 6 carbon atoms within the

straight or branched alkyl group; a mono-, di- or triarylsilyl group each independently having a substituted or unsubstituted aryl group; a trifluoromethyl group; -COM; -COOM; or a -CH₂COOM group (wherein M represents hydrogen, a straight or branched C₁ to C₁₈-alkyl group which may be substituted with one or more hydroxy and/or amino groups, or an aryl group, which may be substituted with one or more halogen, alkyl groups or alkoxy groups which may have one or more heteroatoms; an -NR³⁰R³¹ group (wherein R³⁰ and R³¹ ~~may be the same or different and~~ independently represent a hydrogen atom, a C₁ to C₁₈ straight or branched alkyl group which may be additionally substituted with one or more hydroxy and/or amino groups, a substituted or unsubstituted aryl group which may have one or more heteroatoms); an acyl group; a -CH₂-NR³⁰R³¹ methyleneamino group; a benzyl group which may have one or more heteroatoms in the benzene ring; a methylenecycloalkyl group having 3 to 7 carbon atoms which may have one or more heteroatoms; a physiological amino acid group coupled to a nitrogen atom as an amide; an O-glycoside or N-glycoside having glycoside of which being selected from monosaccharides or disaccharides; or a methylenesulfonate group; R²¹, R²², R²³, R²⁴, R²⁶, R²⁷, R²⁸ and R²⁹ may be the same or different and represent hydrogen; halogen; a hydroxy group; a nitroso group; a nitro group; an alkoxy group; a straight or branched C₁ to C₁₈ alkyl group which may be substituted with one or more hydroxy and/or amino groups; a substituted or unsubstituted aryl group which may have one or more heteroatoms; a substituted or unsubstituted aralkyl group which may have one or more heteroatoms; a substituted or unsubstituted aryloxy group which may have one or more heteroatoms; a substituted or unsubstituted methylenearyloxy group which may have one or more heteroatoms; a cycloalkyl group having 3 to 7 carbon atoms which may have one or more

heteroatoms; a methylenecycloalkyl group having 3 to 7 carbon atoms which may have one or more heteroatoms; a trifluoromethyl group; -COM; -COOM; or a CH₂COOM group (wherein M represents hydrogen, a straight or branched C₁ to C₁₈-alkyl group which may be additionally substituted with one or more hydroxy and/or amino groups, or an aryl group, which may be substituted with one or more halogen atoms, alkyl groups or alkoxy groups which may have one or more heteroatoms); an -NR³⁰R³¹ group (wherein R³⁰ and R³¹ ~~which may be the same or different and~~ independently represent hydrogen, a straight or branched C₁ to C₁₈-alkyl group which may be additionally substituted with one or more hydroxy and/or amino groups, a substituted or unsubstituted aryl group which may have one or more heteroatoms, ~~an acyl group, or form a part of cycloalkyl having 3 to 7 carbon atoms with the nitrogen atom which may have one or more heteroatoms~~); a -CONR³⁰R³¹ group; a hydroxylamino group; a phosphate group; a phosphonate group; a sulfate group; a sulfonate group; a sulfonamide group; an -SO₂NR³⁰R³¹ group; an -N=N-R³² azo group (wherein R³² represents an aromatic group which may be substituted with one or more carboxyl, phosphoryl or sulfonate groups, or an O-glycoside or N-glycoside group having glycoside of which being selected from monosaccharides or disaccharides); or R²⁰ and R²⁴, and R²⁵ and R²⁹ together form a ring which may have one to four CH₂ groups each independently substituted, respectively; Y and Z ~~may be the same or different and~~ independently represent an oxygen atom; a sulfur atom; a selenium atom; a tellurium atom; an NR³³ group (wherein R³³ represents hydrogen, a straight or branched C₁ to C₁₈ alkyl group which may be substituted with one or more carboxyl, phosphoryl or sulfonate groups, a substituted or unsubstituted aryl group which may have one or more heteroatoms, an aralkyl group or a sulfonate group); or -NOR³³],

or a pharmacologically acceptable salt thereof.

17. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 16, wherein the substance that inhibits the activity of GSK-3 is ~~a compound~~ selected from the group consisting of indirubin, 5-iodo-indirubin, 5-bromo-indirubin, 5-chloro-indirubin, 5-fluoro-indirubin, 5-methyl-indirubin, 5-nitro-indirubin, 5-SO₃H-indirubin, 5'-bromo-indirubin, 5-5'-dibromo-indirubin and 5'-bromo-indirubin 5-sulfonic acid,

or a pharmacologically acceptable salt thereof.

18. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 16, wherein the substance that inhibits the activity of GSK-3 is ~~a compound~~ selected from the group consisting of indirubin-3'-monooxime, 5-iodo-indirubin-3'-monooxime and 5-SO₃Na-indirubin-3'-monooxime,

or a pharmacologically acceptable salt thereof.

19. (Currently Amended) The method according to ~~any one of claims 1 to 3~~ claim 16, wherein the substance that inhibits the activity of GSK-3 is indirubin-3'-~~monooxime~~ monooxime,

or a pharmacologically acceptable salt thereof.

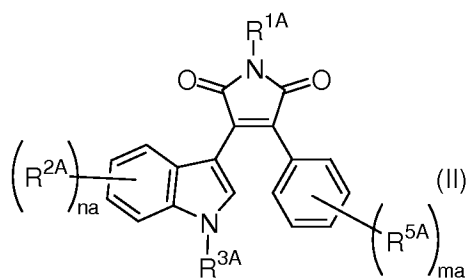
Claims 20-41 (Cancelled)

42. (New) A method of manufacturing a Tuj1 positive neuron which comprises culturing a neural stem cell in the presence of a substance that inhibits glycogen synthase kinase-3 (GSK-3) to allow neogenesis of the neuron, and collecting the neuron from the culture, wherein the substance that inhibits the activity of GSK-3 is siRNA selected from the group consisting of SEQ ID NOS: 15-17.

43. (New) A method of manufacturing a tuj1 positive neuron which comprises culturing a neural stem cell in the presence of an active agent to allow neurogenesis of neuron, and collecting the neuron from the culture, wherein the active agent consists of a 3-aryl-4-indolylmaleimide derivative,

or a pharmacologically acceptable salt thereof.

44. (New) The method according to claim 43, wherein the 3-aryl-4-indolylmaleimide derivative is represented by formula (II):



[wherein na and ma independently represent an integer of 1 to 3; R^{1A} and R^{3A} independently represent hydrogen, substituted or unsubstituted lower alkyl, substituted

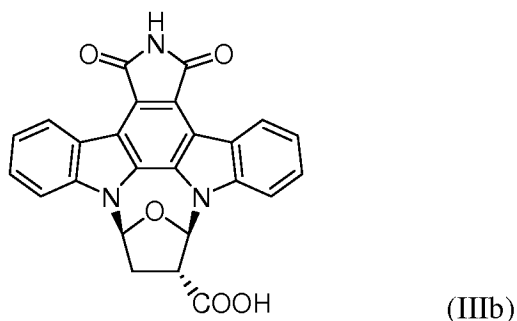
or unsubstituted lower alkenyl, -COR⁶ (wherein R⁶ represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl), -COOR⁷ (wherein R⁷ represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl) or -OR⁸ (wherein R⁸ represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl); R^{2A} and R^{5A} independently represent hydrogen, substituted or unsubstituted lower alkyl, a substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, carboxy, halogen, hydroxy, nitro, amino, or mono- or di-lower alkylamino; and when n and m are 2 or 3, each of R² and R⁵ may be the same or different],

or a pharmacologically acceptable salt thereof.

45. (New) The method according to claim 44, wherein the 3-aryl-4-indolylmaleimide derivative is 3-(2-chlorophenyl)-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-(2,4-dichlorophenyl)-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-(2-chlorophenyl)-4-[1-(3-hydroxypropyl)indole-3-yl]-1H-pyrrole-2,5-dione, or 4-[1-(3-aminopropyl)indole-3-yl]-3-(2-chlorophenyl)-1H-pyrrole-2,5-dione,

or a pharmacologically acceptable salt thereof.

46. (New) The method according to claim 9, wherein the indolocarbazole derivative is represented by formula (IIIb)

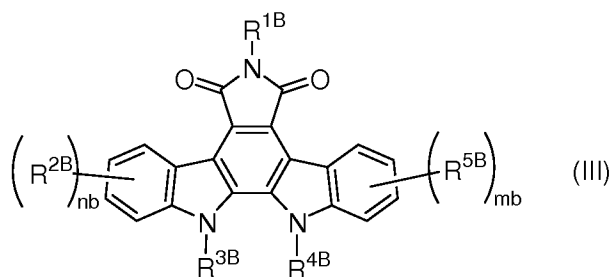


or a pharmacologically acceptable salt thereof.

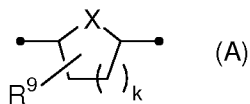
47. (New) A method of manufacturing a *tuj1* positive neuron which comprises culturing a neural stem cell in the presence of a substance that inhibits glycogen synthase kinase-3 (GSK-3) to allow neurogenesis of neuron, and collecting the neuron from the culture, wherein the substance that inhibits the activity of GSK-3 is an indolocarbazole derivative,

or a pharmacologically acceptable salt thereof.

48. (New) The method according to claim 47, wherein the indolocarbazole derivative is represented by formula (III):



[wherein nb and mb independently represent an integer of 1 to 3; R^{1B} represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, $-\text{COR}^6$ (wherein R^6 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl), $-\text{COOR}^7$ (wherein R^7 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl) or $-\text{OR}^8$ (wherein R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl); R^{2B} and R^{5B} independently represent hydrogen, substituted or unsubstituted lower alkyl, a substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, carboxy, halogen, hydroxy, nitro, amino, or mono- or di-lower alkylamino; and when n and m are 2 or 3, each of R^2 and R^5 may be the same or different; R^{3B} and R^{4B} independently represent hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, $-\text{COR}^6$, $-\text{COOR}^7$ or $-\text{OR}^8$, or R^{3B} and R^{4B} together form



(wherein k represents 1 or 2; X represents CH_2 , NH, an oxygen atom or a sulfur atom; R^9 represents hydroxy, carboxy, carbamoyl or lower alkoxycarbonyl)];

or a pharmacologically acceptable salt thereof.

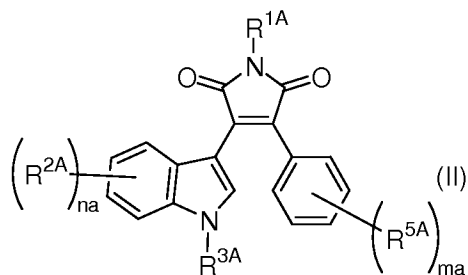
49. (New) A method manufacturing a tuJ1 positive neuron which comprises culturing a neural stem cell in the presence of a substance that inhibits glycogen synthase kinase-3 (GSK-3) to allow neurogenesis of neuron, and collecting the neuron from the culture, wherein the substance that inhibits the activity of GSK-3 is an indolo[3,2-d][1]benzazepin-6(5H)-one derivative,

or a pharmacologically acceptable salt thereof.

50. (New) A method manufacturing a tuJ1 positive neuron which comprises culturing a neural stem cell in the presence of a substance that inhibits glycogen synthase kinase-3 (GSK-3) to allow neurogenesis of neuron, and collecting the neuron from the culture, wherein the substance that inhibits the activity of GSK-3 is an indirubin derivative,

or a pharmacologically acceptable salt thereof.

51. (New) A method of manufacturing a tuJ1 positive neuron which comprises culturing a neural stem cell in the presence of an active agent to allow neurogenesis of neuron, and collecting the neuron from the culture, wherein the active agent comprises a 3-aryl-4-indolylmaleimide derivative represented by formula (II):



[wherein n_a and m_a independently represent an integer of 1 to 3; R^{1A} and R^{3A} independently represent hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, $-COR^6$ (wherein R^6 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl), $-COOR^7$ (wherein R^7 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl) or $-OR^8$ (wherein R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl); R^{2A} and R^{5A} independently represent hydrogen, substituted or unsubstituted lower alkyl, a substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxy carbonyl, substituted or unsubstituted aryl, carboxy, halogen, hydroxy, nitro, amino, or mono- or di-lower alkylamino; and when n and m are 2 or 3, each of R^2 and R^5 may be the same or different],

or a pharmacologically acceptable salt thereof.

52. (New) The method according to claim 51, wherein the 3-aryl-4-indolylmaleimide derivative is 3-(2-chlorophenyl)-4-(1-methylindole-3-yl)-1H-pyrrole-

2,5-dione, 3-(2,4-dichlorophenyl)-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-(2-chlorophenyl)-4-[1-(3-hydroxypropyl)indole-3-yl]-1H-pyrrole-2,5-dione, or 4-[1-(3-aminopropyl)indole-3-yl]-3-(2-chlorophenyl)-1H-pyrrole-2,5-dione,

or a pharmacologically acceptable salt thereof.